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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/572,582	07/13/2007	Bellur S. Prabhakar	21726-103049	2864

23644 7590 07/08/2010

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EXAMINER	
HIBBERT, CATHERINE S	

ART UNIT	PAPER NUMBER
1636	

NOTIFICATION DATE	DELIVERY MODE
07/08/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patent-ch@btlaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/572,582	PRABHAKAR, BELLUR S.	
	Examiner	Art Unit	
	CATHERINE HIBBERT	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21,25 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,25 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/15/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's Amendment to the Claims filed 15 March 2010 is received and entered. This US 10/572,582 application filed 13 July 2007, which is a 371 of PCT/US2004/030986 filed 22 September 2004, claims benefit of 60/505,264 filed 22 September 2003. Claims 1-20, 22-24 and 26 are cancelled. Claim 27 is new. Claims 21, 25 and 27 are pending and under examination.

Information Disclosure Statement

The IDS statement filed 3/15/2010 has been considered by the examiner.

Response to Amendments/Arguments

Any objections and rejections to newly cancelled claims 22-24 and 26 are moot.

Any objections and rejections not repeated herein are withdrawn.

New grounds of rejection necessitated by amendment

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 21, 25 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Al-Zoubi et al in "Contrasting Effects Of IG20 And Its Splice Isoforms, MADD And DENN-SV, On Tumor Necrosis Factor Alpha-Induced Apoptosis And Activation Of Caspase-8 And -3" (Journal Of Biological Chemistry, vol. 276, no. 50, 14 December 2001, entire document, of record) or Efimova et al: "Differential effects of IG20 and its splice isoform, DENN-SV, on cell proliferation and apoptosis" FASEB JOURNAL, vol. 16, no. 5, 22 March 2002, page A1083, of record) in view of Lim and Chow in "Induction of Marked Apoptosis in Mammalian Cancer Cell Lines by Antisense DNA Treatment to Abolish Expression of DENN (Differentially Expressed in Normal and Neoplastic Cells" (Molecular Carcinogenesis, Vol 35, pages 110-126, 2002, made of record in the IDS) and further in view of Thompson in "Application of antisense and siRNAs during preclinical drug development" (DDT Vol. 7, No 17, September 2002, made of record in the IDS).

Currently amended Claim 21 is drawn to a method to increase cancer cell death by modulating expression of human splice variants of *IG20* in the cell, the method comprising decreasing cell replication by administering siRNA to knock down splice variant DENN-SV to the cell. Claim 25 is drawn to the method of Claim 21, further administering chemotherapy to the cancer cell. Claim 27 is drawn to the method of Claim 21, further comprising increasing cancer cell death and slowing cancer cell growth by increasing the expression of splice variant *IG20*.

Efimova et al discloses that the *IG20 gene* (which encodes a pro-apoptotic IG20 protein) is expressed in seven different isoforms in various combinations in both normal and cancer cells and tissues. Furthermore, it is disclosed that HeLa cancer cells transfected with IG20-isoform showed slow growth and enhanced TNF-alpha induced apoptosis, while the HeLa cancer cells transfected with the isoform DENN-SV showed high proliferation and increased resistance to apoptosis. Similar effects were found when HeLa cancer cells were administered various types of chemotherapy treated with vinblastin, etoposide, or gamma irradiation page (e.g.page A1083).

Al-Zoubi et al showed that HeLa cancer cells stably transfected with IG20 showed enhanced susceptibility to TNF-alpha-induced apoptosis, whereas HeLa cells transfected with DENN-SV showed resistance (e.g. pages 47202- 47211).

While the Efimova et al and Al-Zoubi et al references demonstrate that increasing the DENN-SV splicing isoform expression in cancer cells correlated to high proliferation and increased resistance to cancer cell death (i.e. apoptosis) the references fail to teach administering siRNA to knock down splice variant DENN-SV.

Lim and Chow disclose a method to increase cancer cell death by modulating expression of human splice variants of *IG20* in the cancer cells by decreasing cell replication by administering antisense RNA with four separate *DENN*-targeted antisense oligonucleotides (ODNs) to abrogate (i.e. "knock down") *DENN* expression (e.g. abstract) but also fails to disclose the use of siRNA.

Thompson (2002) reviews the state of the prior art regarding the use of siRNA technology and teaches that siRNA technology is known in the art and is often preferred to antisense technology to abrogate/knock-down targeted gene expression (entire article).

One of ordinary skill in the art would have been motivated to use this known siRNA technology for gene silencing/"knock-down" in mammalian cells because Thompson discloses the successful use of 21-22 nucleotides synthetic siRNAs to silence (i.e. knock-down) targeted genes in mammalian cells (page 913, left column, paragraph headed "SiRNA technology").

One of ordinary skill in the art would have been motivated to use this known siRNA technology particularly as a means of gene silencing/"knock-down" in mammalian cells in light of the following Thompson's recitation (page 913, right column, paragraph 4):

> siRNAs have an advantage over antisense in that lower concentrations are needed to achieve levels of knockdown that are comp arable to antisense reagents. Also, siRNAs can be expressed intracellularly from RNA polymerase III promoters [35-37]. This enables the production of stably expressing siRNA cell lines with sustained knockdown of a target and the potential to produce transgenic animals.

Absent evidence to the contrary, one would have a reasonable expectation of success combining the teachings of the art because the use of the siRNA technology for abrogation of specific gene expression in substitution for antisense technology was routinely practiced at the time the invention.

Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result when utilizing the siRNA technology (as taught by Thompson) in combination with the *DENN* gene knock-down methods of Lim and Chow and further in combination with the methods of Efimova et al and Al-Zoubi et al which show the benefits of increasing expression of the splice variant IG20 while decreasing the expression of the splice variant DENN-SV in particular in a method of further administering chemotherapy to cancer cells.

In view of the foregoing, the method of claims 21, 25 and 27, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC *§103(a)*.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CATHERINE HIBBERT whose telephone number is (571)270-3053. The examiner can normally be reached on M-F 8AM-5PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NANCY VOGEL/
Primary Examiner, Art Unit 1636

Catherine Hibbert
Examiner AU1636